REMARKS

Status of Claims

Claims 15-20, 24 and 25 were pending, and claims 15-17 and 24 to the extent they encompassed a modified epoD protein, were under examination. Claims 15-20, 24 and 25 are canceled by this amendment, and new claims 29-44 are added. Support for claims 29-44 is found in the original claims (e.g., claims 15, 16 and 21) and the specification (e.g., page 53, line 25 to page 54, line 5; page 64, 12-17; page 32, line 5-10; page 36, line 17-19; page 37, line 15-18; page 38, lines 1-3; page 39, lines 11-13; page 40, lines 12-21 and 26-27).

Objections under 37 C.F.R. § 1.75(d)(1)

The claims were objected to as presenting an improper Markush group and containing non-elected subject matter. The new claims are directed to the epoD protein subunit of epothilone polyketide synthase, and thus do not read on non-elected subject matter. The objection to claims 15-17, and 24 as allegedly presenting an improper Markush groups is mooted by the cancellation of these claims.

Rejections under 35 U.S.C. § 112, 2nd paragraph

The rejection of the claims as allegedly being indefinite for use of acronyms, for not specifying that the "modified functional epothilone PKS" refers to epoD, and for use of other terms, is mooted by the cancellation of claims 15-17, and 24. The new claims define the acronyms DH, ER, KR and PKS, omit the terms objected to, and are specifically directed to the product of the *epoD* gene of the epothilone PKS gene cluster.

As used in this amendment and as defined in the specification, the term "epothilone polyketide synthase" refers to a multiprotein complex composed of the gene products of the *epoA*, *epoB*, *epoC*, *epoD*, *epoE*, and *epoF* genes (see specification at page 16, lines 1-7) and the term "epoD protein" refers to the product of the *epoD* gene.

Rejections under 35 U.S.C. § 103(a)

Claims 15-17 and 24 were rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of Pat. No. 6,121,029 ("Schupp"), Pat. No. 6,391,594 ("Khosla A"), and PCT publication WO

97/02358 ("Khosla B"). To the extent this rejection is applied to any of the newly added claims, Applicants respectfully traverse.

Schupp is cited as describing a *Sorangium cellulosum* "*epoC*" gene with >98% sequence homology to the *epoD* gene disclosed in the present specification. The Office states the "*epoC* gene taught by Schupp appears to be identical or functionally equivalent to the *epoD* of the instant application." The Applicants respectfully submit that the Schupp reference does not describe (or suggest) any modification of the epoC/D protein and or any epoC/D protein lacking the β-carbonyl modifying activities recited in claim 29, or lacking the specific ketoreductase activities recited in claims 41 and 43.

The Khosla A reference provides guidance for manipulation, modification, and expression of polyketide synthases, not limited to any particular PKS, module or domain. The Khosla A reference does not describe the epothilone PKS or modifications to the *epoD* gene or epoD protein. The Khosla B reference describes synthesis of modified polyketide synthases using cell-expression systems.

The invention encompassed by the claims, as amended herein, is directed to epoD proteins in which specific beta-carbonyl modifying activities have been inactivated. Nothing in the Schupp reference suggests *any* modification of the *epoD* gene product, much less the *specific* modifications claimed by the present inventors. Similarly, neither the Khosla A nor Khosla B references describes or suggests the specific modifications claimed or directs the artisan to make modifications to the epothilone PKS. Taken in combination, there is nothing in the references relied on by the Office that suggests the invention now claimed. The fact that the skilled practitioner reading Khosla A reference would grasp that domains and modules encoded by polyketide synthase genes *can* be modified and manipulated does not render obvious the *particular* modified epoD proteins now claimed. The present invention, directed to specific, useful epoD protein derivatives for which there is no suggestion in the prior art, is a patentable advance over the teachings of the prior art.

Information Disclosure Statement

This response is accompanied by a supplemental information disclosure statement, including references previously submitted but indicated by the Examiner to be missing from the file.

CONCLUSION

If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 300622003110.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

Respectfully submitted,

Dated: March 6, 2003 By: _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please cancel claims 15-20, 24 and 25 without prejudice to future prosecution in this or a related application.

Please add new claims 29-44.